Clinical trial results:
A Multicenter, Randomized, Open-Label, Controlled Trial to Assess the Safety and Tolerability of Lucinactant for Inhalation in Preterm Neonates 26 to 28 Weeks PMA.

Summary

EudraCT number	2015-005624-26
Trial protocol	PL
Global end of trial date	09 July 2017

Results information

Result version number	v1
This version publication date	27 October 2022
First version publication date	27 October 2022
Summary attachment (see zip file)	03-CL-1401 CSR Version 1.0 FINAL (03-CL-1401 CSR Version 1.0 FINAL.pdf)

Trial information

Trial identification

Sponsor protocol code	03-CL-1401

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02528318
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Windtree Therapeutics, Inc.
Sponsor organisation address	2600 Kelly Road, Warrington, United States, 18976
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Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 November 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 July 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the safety and tolerability of lucinactant for inhalation, administered as an aerosolized dose in 4 escalating doses to preterm, neonates 26 to 28 completed weeks PMA with receiving nCPAP for RDS compared with neonates receiving nCPAP alone.

Protection of trial subjects:

A Safety Review Committee was established to review safety data for this study. SRC was formed to evaluate the degree of risk involved in study subject participation within each dosing group to determine if study continuation in accordance with the current protocol held the potential to institute any undue harm, or threat to the safety and welfare of study subjects.
After all active subject within Dosing Group 1 completed Study Day 7, a safety assessment (AEs incl. ADEs, SAEs and additional safety endpoints) was performed. Dosing was allowed to continue to the next higher dosing group (ie. Dosing Group II) immiediately following completion of nerollment within the current dosing group. The SRC provided recommendations following their review of the safety data. This process of continuing to the next higher dosing group and reviewing safety and tolerability was to be continued for the 100 and 150mg TPL/kg group. Subject were followed for safety evaluations until the subect were 36 weeks PMA or were discharged. A final visit ocured at 36 weeks PMA or at time of discharge or withdrawal for all subjects.

Background therapy:

Standard of care (nCPAP alone)

Evidence for comparator: -

Actual start date of recruitment	01 October 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 5
Country: Number of subjects enrolled	Canada: 16
Country: Number of subjects enrolled	Chile: 1
Country: Number of subjects enrolled	United States: 26
Worldwide total number of subjects	48
EEA total number of subjects	5

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	48
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

1.Signed ICF from legally representative
2.Gestational age 26 to 28 weeks PMA
3. Implementation of controlled nCPAP within 90min after birth
4.Spontaneous breathing
5.Chest radiograph consistent with RDS
6.Within first 20hours after birth, required nCPAP of5-6cm H2O and FiO2 of 0,25-0,50 that was clinically indicated for min. 30mins

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

This study was an open-label study to determine the safety and tolerability of lucinactant for inhalation. No blinding or masking procedures were implemented.

Arms

Are arms mutually exclusive?	Yes
Arm title	50mg/kg

Arm description:

Lucinactant for inhalation 50 mg total phospholipids (TPL)/kg with nCPAP (drug-device combination product)
1 repeat dose allowed if repeat dosing criteria are met.

Arm type	Experimental
Investigational medicinal product name	Lucinactant for inhalation
Investigational medicinal product code	
Other name	AEROSURF®
Pharmaceutical forms	Nebuliser suspension
Routes of administration	Inhalation use

Dosage and administration details:

50 mg TPL/kg administered over 30 minutes in conjunction with nCPAP.
1 Repeat dose of 50 mg TPL/kg administered was allowed if repeat dosing criteria were met

Arm title	75mg/kg

Arm description:

Lucinactant inhalation 75 mg TPL/kg with nCPAP (drug-device combination product)
1 repeat dose allowed if repeat dosing criteria are met

Arm type	Experimental
Investigational medicinal product name	Lucinactant for inhalation
Investigational medicinal product code	
Other name	AEROSURF®
Pharmaceutical forms	Nebuliser suspension
Routes of administration	Inhalation use

Dosage and administration details:

75 mg TPL/kg administered over 45 minutes in conjunction with nCPAP
1 repeat dose of 75 mg TPL/kg was allowed if repeat dosing criteria are met

Arm title	100 mg/kg

Arm description:	
Lucinactant fot inhalation 100mg TPL/kg with nCPAP (drug-device combination product) 1 repeat dosing will be allowed if repeat criteria are met.	
Arm type	Experimental
Investigational medicinal product name	Lucinactant for inhalation
Investigational medicinal product code	
Other name	AEROSURF®
Pharmaceutical forms	Nebuliser suspension
Routes of administration	Inhalation use
Dosage and administration details:	
100 mg TPL/kg administered over 60 minutes in conjunction with nCPAP 1 repeat dose ok 100 mg TPL/kg was allowed if repeat dosing criteria are met	
Arm title	nCPAP only
Arm description:	
nCPAP therapy alone	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	50mg/kg	75mg/kg	100 mg/kg
Started	8	8	8
Completed	8	8	8

Number of subjects in period 1	nCPAP only
Started	24
Completed	24

Baseline characteristics

Reporting groups	
Reporting group title	50mg/kg
Reporting group description:	
Lucinactant for inhalation 50 mg total phospholipids (TPL)/kg with nCPAP (drug-device combination product) 1 repeat dose allowed if repeat dosing criteria are met.	
Reporting group title	75mg/kg
Reporting group description:	
Lucinactant inhalation 75 mg TPL/kg with nCPAP (drug-device combination product) 1 repeat dose allowed if repeat dosing criteria are met	
Reporting group title	100 mg/kg
Reporting group description:	
Lucinactant fot inhalation 100mg TPL/kg with nCPAP (drug-device combination product) 1 repeat dosing will be allowed if repeat criteria are met.	
Reporting group title	nCPAP only
Reporting group description:	
nCPAP therapy alone	

Reporting group values	50mg/kg	75mg/kg	100 mg/kg
Number of subjects	8	8	8
Age categorical Units: Subjects			
<=18 years	8	8	8
Between 18 and 65 years	0	0	0
>=65 years	0	0	0
Gender categorical Units: Subjects			
Female	3	5	5
Male	5	3	3
Ethnicity Units: Subjects			
Hispanic or Latino	3	1	2
Not Hispanic or Latino	5	7	6
Unknown or not reported	0	0	0
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	2	0	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	1	2
White	3	5	4
More than one race	0	0	0
Unknown or Not Reported	2	2	1
Region of Enrollment Units: Subjects			
Canada	1	3	4
United States	7	3	4

Poland	0	2	0
Chile	0	0	0

Gestational age			
Gestational age, based on obstetrician's best estimate			
Units: Weeks			
arithmetic mean	27.6	27.2	27.2
standard deviation	± 0.61	± 1.06	± 0.84
Birth Weight			
Units: gram(s)			
arithmetic mean	1052	855	839
standard deviation	± 174.7	± 84.6	± 224.9
Apgar Score at One Minute			
The Apgar Score measures a baby's health by assessing five characteristics (Appearance, Pulse, Grimace, Activity, and Respiration) . Each of the five characteristics are scored from 0 to 2, and the five scores are summed for the Apgar Score. Thus, the Apgar Score ranges from 0 (worst) to 10 (best), and scores over 7 indicate a baby in good health. Apgar Scores are performed at 1 minute and 5 minutes after birth.			
Units: Scores on a scale			
arithmetic mean	5.4	5.5	6.4
full range (min-max)	2 to 9	2 to 8	3 to 8
Apgar Score at Five Minutes			
The Apgar Score measures a baby's health by assessing five characteristics (Appearance, Pulse, Grimace, Activity, and Respiration) . Each of the five characteristics are scored from 0 to 2, and the five scores are summed for the Apgar Score. Thus, the Apgar Score ranges from 0 (worst) to 10 (best), and scores over 7 indicate a baby in good health. Apgar Scores are performed at 1 minute and 5 minutes after birth.			
Units: Scores on a scale			
arithmetic mean	7.8	6.4	8.1
full range (min-max)	7 to 9	1 to 9	6 to 9

Reporting group values	nCPAP only	Total	
Number of subjects	24	48	
Age categorical			
Units: Subjects			
<=18 years	24	48	
Between 18 and 65 years	0	0	
>=65 years	0	0	
Gender categorical			
Units: Subjects			
Female	8	21	
Male	16	27	
Ethnicity			
Units: Subjects			
Hispanic or Latino	7	13	
Not Hispanic or Latino	17	35	
Unknown or not reported	0	0	
Race			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	1	4	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	1	5	

White	20	32	
More than one race	0	0	
Unknown or Not Reported	2	7	
Region of Enrollment Units: Subjects			
Canada	8	16	
United States	12	26	
Poland	3	5	
Chile	1	1	
Gestational age			
Gestational age, based on obstetrician's best estimate			
Units: Weeks			
arithmetic mean	27.5		
standard deviation	± 0.76	-	
Birth Weight Units: gram(s)			
arithmetic mean	1005		
standard deviation	± 238.8	-	
Apgar Score at One Minute			
The Apgar Score measures a baby's health by assessing five characteristics (Appearance, Pulse, Grimace, Activity, and Respiration) . Each of the five characteristics are scored from 0 to 2, and the five scores are summed for the Apgar Score. Thus, the Apgar Score ranges from 0 (worst) to 10 (best), and scores over 7 indicate a baby in good health. Apgar Scores are performed at 1 minute and 5 minutes after birth.			
Units: Scores on a scale			
arithmetic mean	5.8		
full range (min-max)	1 to 9	-	
Apgar Score at Five Minutes			
The Apgar Score measures a baby's health by assessing five characteristics (Appearance, Pulse, Grimace, Activity, and Respiration) . Each of the five characteristics are scored from 0 to 2, and the five scores are summed for the Apgar Score. Thus, the Apgar Score ranges from 0 (worst) to 10 (best), and scores over 7 indicate a baby in good health. Apgar Scores are performed at 1 minute and 5 minutes after birth.			
Units: Scores on a scale			
arithmetic mean	7.9		
full range (min-max)	5 to 9	-	

End points

End points reporting groups

Reporting group title	50mg/kg
Reporting group description:	
Lucinactant for inhalation 50 mg total phospholipids (TPL)/kg with nCPAP (drug-device combination product) 1 repeat dose allowed if repeat dosing criteria are met.	
Reporting group title	75mg/kg
Reporting group description:	
Lucinactant inhalation 75 mg TPL/kg with nCPAP (drug-device combination product) 1 repeat dose allowed if repeat dosing criteria are met	
Reporting group title	100 mg/kg
Reporting group description:	
Lucinactant fot inhalation 100mg TPL/kg with nCPAP (drug-device combination product) 1 repeat dosing will be allowed if repeat criteria are met.	
Reporting group title	nCPAP only
Reporting group description:	
nCPAP therapy alone	

Primary: Number of Participants With Peri-Dosing Adverse Events - Initial Dose

End point title	Number of Participants With Peri-Dosing Adverse Events - Initial Dose[1]
End point description:	
Number of Participants with adverse events that were experienced during the initial study treatment Peri-dosing events are events that occur during study treatment. Since this was an open-label study, no peri-dosing events were recorded for nCPAP alone. Any adverse events that occurred during the corresponding time for nCPAP alone were recorded as adverse events but not peri-dosing events.	
End point type	Primary
End point timeframe:	
Randomization to 24 Hours Post Randomization	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Because no a priori statistical analyses were conducted in this study, no statistical analysis have been specified

End point values	50mg/kg	75mg/kg	100 mg/kg	nCPAP only
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	8	8	24[2]
Units: Participants				
number (not applicable)				
Bradycardia	0	2	1	0
Desaturation	1	2	3	0
Gagging/regurgitation	0	0	0	0
Apnea	1	1	1	0
Pallor	0	0	0	0

Notes:

[2] - There was no dosing in this group (no intervention, standard of care)

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Air Leak

End point title	Number of Participants With Air Leak[3]

End point description:

Number of participants with air leak (includes pneumothorax, pulmonary interstitial emphysema (PIE), pneumomediastinum, pneumopericardium, subcutaneous emphysema)
This dose-escalation study was terminated after completion of the 100 mg/kg group for administrative purposes. No participants were enrolled in the 150 mg/kg group or received 150 mg/kg.

End point type	Primary

End point timeframe:

7 days

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Because no a priori statistical analyses were conducted in this study, no statistical analysis have been specified

End point values	50mg/kg	75mg/kg	100 mg/kg	nCPAP only
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	8	8	24
Units: Participants				
number (not applicable)	3	0	2	4

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Worsening of Respiratory Status Criteria

End point title	Number of Participants With Worsening of Respiratory Status Criteria

End point description:

Number of participants with worsening in one of 12 respiratory status criteria through 72 hours post randomization (need for additional surfactant therapy, desaturation < 80%, heart rate < 100 bpm, sustained fraction of inspired oxygen (FiO2) > 0.50, arterial carbon dioxide (PCO2) > 65 mmHg, sustained apnea, persistent arterial pH < 7.2, intubation for any reason, nCPAP > 7 cmH2O, initiation of intermittent positive pressure ventilation, death, principal investigator determination of worsening status).
Intent-to-treat population.
This dose-escalation study was terminated after completion of the 100 mg/kg group for administrative purposes. No participants were enrolled in the 150 mg/kg group or received 150 mg/kg.

End point type	Secondary

End point timeframe:

Randomization to 72 Hours Post Randomization

End point values	50mg/kg	75mg/kg	100 mg/kg	nCPAP only
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	8	8	24
Units: Participants				
number (not applicable)	6	7	6	18

Statistical analyses

No statistical analyses for this end point

Secondary: Bronchopulmonary Dysplasia

End point title	Bronchopulmonary Dysplasia

End point description:

Number of participants with bronchopulmonary dysplasia (BPD) and number of participants alive and without BPD at 36 weeks post-menstrual age (PMA)
This dose-escalation study was terminated after completion of the 100 mg/kg group for administrative purposes. No participants were enrolled in the 150 mg/kg group or received 150 mg/kg.

End point type	Secondary

End point timeframe:

Randomization to 36 weeks PMA

End point values	50mg/kg	75mg/kg	100 mg/kg	nCPAP only
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	8	8	24
Units: Participants				
number (not applicable)				
BPD	0	0	0	6
Alive and without BPD	7	7	8	18

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Nasal Continuous Positive Airway Pressure (nCPAP) Failure

End point title	Number of Participants With Nasal Continuous Positive Airway Pressure (nCPAP) Failure

End point description:

Participants who required intubation for mechanical ventilation or surfactant administration were defined as having failed nCPAP.

This dose-escalation study was terminated after completion of the 100 mg/kg group for administrative purposes. No participants were enrolled in the 150 mg/kg group or received 150 mg/kg.

End point type	Secondary

End point timeframe:

Randomization to 72 Hours Post Randomization

End point values	50mg/kg	75mg/kg	100 mg/kg	nCPAP only
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	8	8	24
Units: Participants				
number (not applicable)	5	7	5	16

Statistical analyses

No statistical analyses for this end point

Secondary: Death

End point title	Death

End point description:

Number of participants who died during the study.
This dose-escalation study was terminated after completion of the 100 mg/kg group for administrative purposes. No participants were enrolled in the 150 mg/kg group or received 150 mg/kg.

End point type	Secondary

End point timeframe:

Randomization to 36 weeks PMA

End point values	50mg/kg	75mg/kg	100 mg/kg	nCPAP only
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	8	8	24
Units: Participants				
number (not applicable)	1	1	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: FiO2

End point title	FiO2

End point description:

Observed and change from baseline measurements for fraction of inspired oxygen (FiO2). Values represent the amount (fraction) of oxygen in the air the participant inspires; the values themselves do not have units. The normal amount of oxygen in air ("room air") is 21%, or 0.21.
This dose-escalation study was terminated after completion of the 100 mg/kg group for administrative purposes. No participants were enrolled in the 150 mg/kg group or received 150 mg/kg.

Safety population

End point type	Secondary

End point timeframe:

Randomization to 72 hours post randomization

End point values	50mg/kg	75mg/kg	100 mg/kg	nCPAP only
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	8	8	24
Units: Fraction of oxygen in inspired air				
arithmetic mean (standard deviation)				
Baseline (Randomization)	0.31 (± 0.058)	0.33 (± 0.071)	0.37 (± 0.072)	0.32 (± 0.061)
60 minutes post randomization - observed	0.31 (± 0.064)	0.35 (± 0.063)	0.37 (± 0.090)	0.34 (± 0.159)
60 minutes post randomization - change from baseli	0.01 (± 0.010)	0.02 (± 0.024)	0.01 (± 0.044)	0.01 (± 0.162)
3 hours post randomization - observed	0.37 (± 0.191)	0.37 (± 0.120)	0.37 (± 0.107)	0.29 (± 0.082)
3 hours post randomization - change from baseline	0.06 (± 0.154)	0.00 (± 0.066)	0.00 (± 0.047)	-0.03 (± 0.082)
12 hours post randomization - observed	0.30 (± 0.114)	0.30 (± 0.117)	0.30 (± 0.068)	0.33 (± 0.181)
12 hours post randomization - change from baseline	-0.02 (± 0.137)	-0.07 (± 0.074)	-0.08 (± 0.090)	0.00 (± 0.172)
24 hours post randomization - observed	0.28 (± 0.093)	0.25 (± 0.044)	0.28 (± 0.077)	0.29 (± 0.143)
24 hours post randomization - change from baseline	-0.03 (± 0.072)	-0.09 (± 0.046)	-0.08 (± 0.105)	-0.04 (± 0.140)
48 hours post randomization - observed	0.28 (± 0.058)	0.24 (± 0.038)	0.23 (± 0.071)	0.31 (± 0.188)
48 hours post randomization - change from baseline	-0.03 (± 0.083)	-0.09 (± 0.075)	-0.09 (± 0.091)	-0.02 (± 0.191)
72 hours post randomization - observed	0.3 (± 0.105)	0.23 (± 0.023)	0.25 (± 0.050)	0.27 (± 0.119)
72 hours post randomisation - change from baseline	-0.02 (± 0.133)	-0.10 (± 0.071)	-0.12 (± 0.066)	-0.05 (± 0.133)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Complications of Prematurity

End point title	Number of Participants With Complications of Prematurity

End point description:

Number of participants with pre-specified common complications of prematurity.
The study was terminated after completion of the 100 mg/kg group for administrative purposes. No participants were enrolled in the 150mg/kg group or received a 150mg/kg dose.
Safety population.

End point type	Secondary

End point timeframe:

Randomization to 36 weeks PMA

End point values	50mg/kg	75mg/kg	100 mg/kg	nCPAP only
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	8	8	24
Units: Participants				
number (not applicable)				
Subject with any complication	8	7	7	22
Acquired sepsis	2	2	2	5
Apnea	8	5	6	19
Cystic Periventricular Leukomalcia	0	0	0	1
Patent Ductus Arteriosus	3	3	4	10
Pulmonary Hemorrhage	1	0	1	1
Intraventicular Hemorrhage	0	1	3	4
Necrotizing Enterocolitis	1	1	1	1
Retinopathy of Prematurity	2	1	1	9

Statistical analyses

No statistical analyses for this end point

Other pre-specified: nCPAP Failure Without Treatment Interruptions

End point title	nCPAP Failure Without Treatment Interruptions

End point description:

Number of subjects requiring mechanical ventilation or surfactant administration (nCPAP failure) but did not have a treatment interruption
The study was terminated after completion of the 100 mg/kg group for administrative purposes. No participants were enrolled in the 150 mg/kg group.

End point type	Other pre-specified

End point timeframe:

Randomization to 72 Hours Post Randomization

End point values	50mg/kg	75mg/kg	100 mg/kg	nCPAP only
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	3	6	24
Units: Participants				
number (not applicable)	4	3	3	16

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From randomization to 36 weeks PMA

Adverse event reporting additional description:

This dose-escalation study was terminated after completion of the 100 mg/kg group for administrative purposes. No participants were enrolled in the 150 mg/kg group or received 150 mg/kg.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	50 mg/kg

Reporting group description:

Lucinactant for inhalation 50 mg TPL/kg with nCPAP

1 repeat dose allowed if repeat dosing criteria are met.

Lucinactant for inhalation: Lucinactant for inhalation refers to the active investigational agent, lucinactant, in combination with the investigational delivery device (drug-device combination product)

Reporting group title	75 mg/kg

Reporting group description:

Lucinactant for inhalation 75 mg TPL/kg with nCPAP

1 repeat dose allowed if repeat dosing criteria are met.

Lucinactant for inhalation: Lucinactant for inhalation refers to the active investigational agent, lucinactant, in combination with the investigational delivery device (drug-device combination product)

Reporting group title	100 mg/kg

Reporting group description:

Lucinactant for inhalation 100 mg TPL/kg with nCPAP

1 repeat dose allowed if repeat dosing criteria are met.

Lucinactant for inhalation: Lucinactant for inhalation refers to the active investigational agent, lucinactant, in combination with the investigational delivery device (drug-device combination product)

Reporting group title	nCPAP alone

Reporting group description:

nCPAP therapy alone

Serious adverse events	50 mg/kg	75 mg/kg	100 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 8 (50.00%)	3 / 8 (37.50%)	2 / 8 (25.00%)
number of deaths (all causes)	1	1	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Hepatic haemorrhage			

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal injury	Additional description: Laryngeal trauma due to intubation		
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic liver injury	Additional description: Liver laceration		
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Shock	Additional description: refractory shock		
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Intraventricular haemorrhage neonatal			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 8 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrotising enterocolitis neonatal			

subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Neonatal respiratory distress syndrome			
subjects affected / exposed	0 / 8 (0.00%)	2 / 8 (25.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neonatal respiratory failure			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia neonatal			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastric perforation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumoperitoneum			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Respiratory, thoracic and mediastinal disorders			
Apnoea neonatal			

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neonatal respiratory failure			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis neonatal			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	nCPAP alone		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 24 (25.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Hepatic haemorrhage			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Laryngeal injury	Additional description: Laryngeal trauma due to intubation		

subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Traumatic liver injury	Additional description: Liver laceration		
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Shock	Additional description: refractory shock		
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardio-respiratory arrest			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Intraventricular haemorrhage neonatal			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Necrotising enterocolitis neonatal			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neonatal respiratory distress syndrome			

subjects affected / exposed	1 / 24 (4.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neonatal respiratory failure				
subjects affected / exposed	0 / 24 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia neonatal				
subjects affected / exposed	1 / 24 (4.17%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Gastric perforation				
subjects affected / exposed	1 / 24 (4.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal perforation				
subjects affected / exposed	1 / 24 (4.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumoperitoneum				
subjects affected / exposed	0 / 24 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Apnoea neonatal				
subjects affected / exposed	1 / 24 (4.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neonatal respiratory failure				
subjects affected / exposed	1 / 24 (4.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Pneumothorax			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis neonatal			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	50 mg/kg	75 mg/kg	100 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 8 (100.00%)	8 / 8 (100.00%)	8 / 8 (100.00%)
Vascular disorders			
Haemangioma			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	1 / 8 (12.50%)	2 / 8 (25.00%)	0 / 8 (0.00%)
occurrences (all)	1	2	0
Pregnancy, puerperium and perinatal conditions			
Agitation neonatal			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Bradycardia neonatal			

subjects affected / exposed	0 / 8 (0.00%)	5 / 8 (62.50%)	3 / 8 (37.50%)
occurrences (all)	0	7	5
Fixed bowel loop			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Intraventricular haemorrhage neonatal			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Jaundice neonatal			
subjects affected / exposed	5 / 8 (62.50%)	3 / 8 (37.50%)	1 / 8 (12.50%)
occurrences (all)	5	3	1
Necrotising enterocolitis neonatal			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Neonatal respiratory distress syndrome			
subjects affected / exposed	1 / 8 (12.50%)	2 / 8 (25.00%)	2 / 8 (25.00%)
occurrences (all)	1	2	3
Periventricular haemorrhage neonatal			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Retinopathy of prematurity			
subjects affected / exposed	2 / 8 (25.00%)	1 / 8 (12.50%)	1 / 8 (12.50%)
occurrences (all)	2	1	1
Small for dates baby			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Endotracheal intubation complication			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Face oedema			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Hypothermia			

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Oedema			
subjects affected / exposed	3 / 8 (37.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Pain			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Apnoea neonatal			
subjects affected / exposed	7 / 8 (87.50%)	4 / 8 (50.00%)	6 / 8 (75.00%)
occurrences (all)	7	5	9
Bronchopulmonary dysplasia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Chronic respiratory failure			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Hypercapnia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Nasal discomfort			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Nasal inflammation			
subjects affected / exposed	2 / 8 (25.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Nasal mucosal ulcer			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Neonatal respiratory failure			

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Neonatal tachypnoea			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Pneumothorax			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pulmonary haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Pulmonary hypertension			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pulmonary interstitial emphysema syndrome			
subjects affected / exposed	3 / 8 (37.50%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	3	0	1
Pulmonary oedema neonatal			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Respiratory acidosis			
subjects affected / exposed	2 / 8 (25.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Respiratory alkalosis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Respiratory tract haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Investigations			
Anticonvulsant drug level above therapeutic			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood urea increased			

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Cardiac murmur			
subjects affected / exposed	2 / 8 (25.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	2	1	0
Coagulation time prolonged			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Neutrophil count increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Oxygen saturation decreased			
subjects affected / exposed	2 / 8 (25.00%)	4 / 8 (50.00%)	6 / 8 (75.00%)
occurrences (all)	3	6	11
PO2 increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Reticulocyte count increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Blister			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Ear abrasion			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Infusion site extravasation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Laceration			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Skin abrasion			

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Tracheal injury			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Congenital, familial and genetic disorders			
Atrial septal defect			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Cardiac septal defect			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hydrocele			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Patent ductus arteriosus			
subjects affected / exposed	3 / 8 (37.50%)	3 / 8 (37.50%)	4 / 8 (50.00%)
occurrences (all)	3	3	4
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Nervous system disorders			
Hypotonia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Lethargy			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Periventricular leukomalacia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Seizure			

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia neonatal			
subjects affected / exposed	6 / 8 (75.00%)	4 / 8 (50.00%)	2 / 8 (25.00%)
occurrences (all)	6	6	2
Bandaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Coagulopathy			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Leukocystosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Thrombocytopenia			
subjects affected / exposed	2 / 8 (25.00%)	2 / 8 (25.00%)	0 / 8 (0.00%)
occurrences (all)	2	2	0
Thrombocytosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Constipation			

subjects affected / exposed	5 / 8 (62.50%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	13	0	1
Gastric haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Gastric hypomotility			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal hypomotility			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Haematemesis			
subjects affected / exposed	2 / 8 (25.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Inguinal hernia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Salivary hypersecretion			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Umbilical hernia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Vomiting			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Hepatobiliary disorders			
Cholestasis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Gallbladder disorder			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Skin and subcutaneous tissue disorders			
Dermatitis diaper			
subjects affected / exposed	4 / 8 (50.00%)	2 / 8 (25.00%)	1 / 8 (12.50%)
occurrences (all)	5	2	1
Rash			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Azotaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Oliguria			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Renal failure			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Bacterial disease carrier			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 8 (25.00%)
occurrences (all)	0	0	2
Conjunctivitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Enterococcal sepsis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Fungal skin infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Nosocomial infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Pneumonia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Pneumonia klebsiella			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pneumonia staphylococcal			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Sepsis neonatal			
subjects affected / exposed	1 / 8 (12.50%)	1 / 8 (12.50%)	1 / 8 (12.50%)
occurrences (all)	1	1	1
Septic shock			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection enterococcal			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Urosepsis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Electrolyte imbalance			

subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Feeding intolerance			
subjects affected / exposed	3 / 8 (37.50%)	1 / 8 (12.50%)	1 / 8 (12.50%)
occurrences (all)	3	1	1
Fluid retention			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hypercalcaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Hyperchloraemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Hyperglycaemia			
subjects affected / exposed	1 / 8 (12.50%)	2 / 8 (25.00%)	0 / 8 (0.00%)
occurrences (all)	1	2	0
Hyperkalaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hypermagnesaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Hypernatraemia			
subjects affected / exposed	1 / 8 (12.50%)	2 / 8 (25.00%)	0 / 8 (0.00%)
occurrences (all)	1	2	0
Hypertriglyceridaemia			
subjects affected / exposed	1 / 8 (12.50%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hypochloraemia			

subjects affected / exposed	2 / 8 (25.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	2	1	0
Hypokalaemia			
subjects affected / exposed	0 / 8 (0.00%)	2 / 8 (25.00%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Hypomagnesaemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Hyponatraemia			
subjects affected / exposed	3 / 8 (37.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Hypophosphataemia			
subjects affected / exposed	2 / 8 (25.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Hypovolaemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Metabolic acidosis			
subjects affected / exposed	3 / 8 (37.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Metabolic alkalosis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Osteopenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Vitamin D deficiency			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Hypoglycaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	nCPAP alone		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 24 (100.00%)		

Vascular disorders			
Haemangioma			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Hypertension			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Hypotension			
subjects affected / exposed	4 / 24 (16.67%)		
occurrences (all)	7		
Pregnancy, puerperium and perinatal conditions			
Agitation neonatal			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Bradycardia neonatal			
subjects affected / exposed	9 / 24 (37.50%)		
occurrences (all)	9		
Fixed bowel loop			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Intraventricular haemorrhage neonatal			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Jaundice neonatal			
subjects affected / exposed	11 / 24 (45.83%)		
occurrences (all)	12		
Necrotising enterocolitis neonatal			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Neonatal respiratory distress syndrome			
subjects affected / exposed	9 / 24 (37.50%)		
occurrences (all)	12		
Periventricular haemorrhage neonatal			

subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Retinopathy of prematurity			
subjects affected / exposed	9 / 24 (37.50%)		
occurrences (all)	9		
Small for dates baby			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
General disorders and administration site conditions			
Endotracheal intubation complication			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Face oedema			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Hypothermia			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Oedema			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Pain			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Apnoea neonatal			
subjects affected / exposed	19 / 24 (79.17%)		
occurrences (all)	21		
Bronchopulmonary dysplasia			
subjects affected / exposed	7 / 24 (29.17%)		
occurrences (all)	8		

Chronic respiratory failure				
subjects affected / exposed	0 / 24 (0.00%)			
occurrences (all)	0			
Hypercapnia				
subjects affected / exposed	2 / 24 (8.33%)			
occurrences (all)	4			
Nasal discomfort				
subjects affected / exposed	1 / 24 (4.17%)			
occurrences (all)	1			
Nasal inflammation				
subjects affected / exposed	2 / 24 (8.33%)			
occurrences (all)	2			
Nasal mucosal ulcer				
subjects affected / exposed	0 / 24 (0.00%)			
occurrences (all)	0			
Neonatal respiratory failure				
subjects affected / exposed	1 / 24 (4.17%)			
occurrences (all)	1			
Neonatal tachypnoea				
subjects affected / exposed	2 / 24 (8.33%)			
occurrences (all)	3			
Pneumothorax				
subjects affected / exposed	1 / 24 (4.17%)			
occurrences (all)	1			
Pulmonary haemorrhage				
subjects affected / exposed	1 / 24 (4.17%)			
occurrences (all)	1			
Pulmonary hypertension				
subjects affected / exposed	1 / 24 (4.17%)			
occurrences (all)	1			
Pulmonary interstitial emphysema syndrome				
subjects affected / exposed	3 / 24 (12.50%)			
occurrences (all)	3			
Pulmonary oedema neonatal				

subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Respiratory acidosis			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	2		
Respiratory alkalosis			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	2		
Respiratory tract haemorrhage			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Investigations			
Anticonvulsant drug level above therapeutic			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Blood urea increased			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Cardiac murmur			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Coagulation time prolonged			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Neutrophil count increased			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Oxygen saturation decreased			
subjects affected / exposed	9 / 24 (37.50%)		
occurrences (all)	11		
PO2 increased			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Reticulocyte count increased			

subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Blister			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Ear abrasion			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Infusion site extravasation			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Laceration			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Skin abrasion			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Tracheal injury			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Congenital, familial and genetic disorders			
Atrial septal defect			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Cardiac septal defect			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Hydrocele			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Patent ductus arteriosus			
subjects affected / exposed	10 / 24 (41.67%)		
occurrences (all)	10		

Cardiac disorders			
Arrhythmia			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Tachycardia			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Hypotonia			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Lethargy			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Periventricular leukomalacia			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Seizure			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	2		
Blood and lymphatic system disorders			
Anaemia neonatal			
subjects affected / exposed	12 / 24 (50.00%)		
occurrences (all)	16		
Bandaemia			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Coagulopathy			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Leukocystosis			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Leukopenia			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Neutropenia			

subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Thrombocytopenia			
subjects affected / exposed	4 / 24 (16.67%)		
occurrences (all)	4		
Thrombocytosis			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Gastric haemorrhage			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Gastric hypomotility			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Gastrointestinal hypomotility			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Haematemesis			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Inguinal hernia			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		

Salivary hypersecretion subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0		
Umbilical hernia subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0		
Vomiting subjects affected / exposed occurrences (all)	1 / 24 (4.17%) 1		
Hepatobiliary disorders			
Cholestasis subjects affected / exposed occurrences (all)	3 / 24 (12.50%) 3		
Gallbladder disorder subjects affected / exposed occurrences (all)	1 / 24 (4.17%) 1		
Skin and subcutaneous tissue disorders			
Dermatitis diaper subjects affected / exposed occurrences (all)	1 / 24 (4.17%) 1		
Rash subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2		
Renal and urinary disorders			
Azotaemia subjects affected / exposed occurrences (all)	1 / 24 (4.17%) 1		
Haematuria subjects affected / exposed occurrences (all)	1 / 24 (4.17%) 1		
Oliguria subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2		
Renal failure subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 3		
Endocrine disorders			

Adrenal insufficiency				
subjects affected / exposed	1 / 24 (4.17%)			
occurrences (all)	1			
Infections and infestations				
Bacteraemia				
subjects affected / exposed	1 / 24 (4.17%)			
occurrences (all)	1			
Bacterial disease carrier				
subjects affected / exposed	0 / 24 (0.00%)			
occurrences (all)	0			
Conjunctivitis				
subjects affected / exposed	1 / 24 (4.17%)			
occurrences (all)	1			
Enterococcal sepsis				
subjects affected / exposed	1 / 24 (4.17%)			
occurrences (all)	1			
Fungal skin infection				
subjects affected / exposed	1 / 24 (4.17%)			
occurrences (all)	1			
Nosocomial infection				
subjects affected / exposed	0 / 24 (0.00%)			
occurrences (all)	0			
Pneumonia				
subjects affected / exposed	3 / 24 (12.50%)			
occurrences (all)	3			
Pneumonia klebsiella				
subjects affected / exposed	1 / 24 (4.17%)			
occurrences (all)	1			
Pneumonia staphylococcal				
subjects affected / exposed	1 / 24 (4.17%)			
occurrences (all)	1			
Sepsis neonatal				
subjects affected / exposed	4 / 24 (16.67%)			
occurrences (all)	4			
Septic shock				

subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0		
Urinary tract infection subjects affected / exposed occurrences (all)	1 / 24 (4.17%) 2		
Urinary tract infection enterococcal subjects affected / exposed occurrences (all)	1 / 24 (4.17%) 1		
Urosepsis subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0		
Metabolism and nutrition disorders Dehydration subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0		
Electrolyte imbalance subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0		
Feeding intolerance subjects affected / exposed occurrences (all)	1 / 24 (4.17%) 1		
Fluid retention subjects affected / exposed occurrences (all)	1 / 24 (4.17%) 1		
Hypercalcaemia subjects affected / exposed occurrences (all)	1 / 24 (4.17%) 1		
Hyperchloraemia subjects affected / exposed occurrences (all)	3 / 24 (12.50%) 3		
Hyperglycaemia subjects affected / exposed occurrences (all)	3 / 24 (12.50%) 5		
Hyperkalaemia subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2		

Hypermagnesaemia				
subjects affected / exposed	0 / 24 (0.00%)			
occurrences (all)	0			
Hypernatraemia				
subjects affected / exposed	4 / 24 (16.67%)			
occurrences (all)	5			
Hypertriglyceridaemia				
subjects affected / exposed	2 / 24 (8.33%)			
occurrences (all)	3			
Hypoalbuminaemia				
subjects affected / exposed	3 / 24 (12.50%)			
occurrences (all)	3			
Hypocalcaemia				
subjects affected / exposed	2 / 24 (8.33%)			
occurrences (all)	2			
Hypochloraemia				
subjects affected / exposed	3 / 24 (12.50%)			
occurrences (all)	4			
Hypokalaemia				
subjects affected / exposed	3 / 24 (12.50%)			
occurrences (all)	4			
Hypomagnesaemia				
subjects affected / exposed	1 / 24 (4.17%)			
occurrences (all)	1			
Hyponatraemia				
subjects affected / exposed	7 / 24 (29.17%)			
occurrences (all)	7			
Hypophosphataemia				
subjects affected / exposed	1 / 24 (4.17%)			
occurrences (all)	1			
Hypovolaemia				
subjects affected / exposed	0 / 24 (0.00%)			
occurrences (all)	0			
Metabolic acidosis				
subjects affected / exposed	5 / 24 (20.83%)			
occurrences (all)	5			

Metabolic alkalosis subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0		
Osteopenia subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2		
Vitamin D deficiency subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0		
Hypoglycaemia subjects affected / exposed occurrences (all)	3 / 24 (12.50%) 3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 September 2015	Rationale for protocol amendment - additional requirement of meeting criteria at treatment initiation added - additional clarification on repeat dose - typo corrections - clarification of "completion of study" - SRC approval not required to advance to next dosing level - repeat dosing criteria changed - concomitant medications - additional clarifications added - supplement to the instruction for ADP returns - clarification of when SRC meeting would be held following a death - clarification of peri-dosing events

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
09 July 2017	The sponsor of study 03-CL-1401, Windtree Therapeutics, Inc. has made a decision to terminate the dose-escalation study early after the completion of enrollment into Dose Group 3 3. It was anticipated 64 subjects would be enrolled into the study in four dose groups; however, only 48 subjects were enrolled (Dose Groups 1,2,3; n=16 per group). The decision to terminate the study early was taken to incorporate learning from this study into a redesigned trial to continue studying neonates in the 26-28 week gestational age. To this end, sponsor planned to study the 26-28 week GA patients in the amendment (Amendment 2) to the 03-CL-1202 study. A preliminary review of the data through Dose Group 3 has shown no safety signal of concern and the overall safety and tolerability profile was generally similar to the control group treated with nCPAP alone. A maximum tolerated dose was not established, the overall objective of the study was met. Early termination of 03-CL-1401 study has no effect on the overall risk-benefit assessment of lucinactant for inhalation. Last subject randomized into the study was on 16 May 2017 and was followed through study completion, which is 36 weeks PMA (9 July 2017)	-

Notes:

Limitations and caveats

None reported